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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,026	07/30/2001	Rosanne M. Crooke	ISPH-0588	1035

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EXAMINER

GIBBS, TERRA C

ART UNIT	PAPER NUMBER
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1635

12

DATE MAILED: 05/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No. 09/918,026	Applicant(s) CROOKE ET AL.	
	Examiner Terra C. Gibbs	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2 and 4-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, and 4-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

Applicant's Amendment and Response to Restriction Requirement, filed February 20, 2003 in Paper No. 11 is acknowledged.

This Office Action is a response to Applicant's Amendment and Remarks filed February 20, 2003 in Paper No. 11. Claims 11 and 15-20 have been canceled. Claim 1 has been amended.

Claims 1, 2, and 4-14 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2 and 4-14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cases et al. [WO 99/67368] and Sturley [WO 97/45439] in further view of Baracchini et al. [U.S. Patent No. 5801154] and Fritz et al. (Journal of Colloid and Interface Science, 1997 Vol. 195:272-288), for reasons of record set forth in the previous office action of mailed November 19, 2002 in Paper No. 10.

Applicant's arguments, filed February 20, 2003, have been fully considered but they are not persuasive. Applicants, in response to the previous Office Action, argue that claim 1 has been amended to recite specific regions of acyl CoA cholesterol acetyltransferase-2 targeted by antisense compounds which are not disclosed by Cases et al. or Sturley. Applicants argue that

while Cases et al. and Sturley mention the idea of using antisense compounds as a way to modulate the activity of acyl CoA cholesterol acetyltransferase-2, nowhere do the references provide data showing the successful inhibition of gene expression using antisense compounds. Applicants further argue that Cases et al. and Sturley do not teach or suggest antisense compounds which are targeted to specific regions of acyl CoA cholesterol acetyltransferase-2. Applicants also argue that Baracchini et al. teach modifications to antisense oligonucleotides to enhance activity, but do not teach or suggest the use of antisense compounds targeted to acyl CoA cholesterol acetyltransferase-2 (SEQ ID NO:3). Applicants further argue that Fritz et al. disclose cationic polystyrene nanoparticles as carrier systems for antisense compounds in general, but do not teach or suggest the use of antisense compounds targeted to acyl CoA cholesterol acetyltransferase-2 (SEQ ID NO:3).

Applicant's arguments have been carefully considered but are not considered persuasive because the criteria for a 103 rejection is based on three factors: (1) obviousness (2) motivation and (3) expectation of success. In totality, the references render the instant application obvious and demonstrate that one of ordinary skill in the art would have been motivated and expected success in making and using the current invention at the time of filing. As argued in the Office action mailed November 19, 2002, it would have been obvious and one would have been motivated to make antisense oligonucleotides encoding acyl CoA cholesterol acetyltransferase-2 since the prior art has asserted that acyl CoA cholesterol acyltransferase is an enzyme involved in cholesterol esterification and cholesterol absorption (Cases et al.). As further argued, one of ordinary skill in the art would have had a reasonable expectation of success in making antisense oligonucleotides targeting acyl CoA cholesterol acyltransferase-2 since Cases et al. taught an

Art Unit: 1635

agent consisting of a nucleic acid sequence consisting of all or a part of acyl CoA cholesterol acyltransferase-2 will decrease or down regulate the expression of acyl CoA cholesterol acyltransferase-2 and Sturley taught a nucleic acid having a sequence complementary to an isolated nucleic acid which encodes an acyl CoA cholesterol acyltransferase-2 and prevents translation of the mRNA. As further argued, one of ordinary skill in the art would have been motivated to modify antisense oligonucleotides since the prior art has taught the desirability of such oligonucleotides are often preferred over native forms because of enhanced cellular uptake, enhanced affinity for nucleic acid target, increased stability in the presence of nucleases and the exhibition of high colloidal stability with low toxic side effects as required for biological experiments (Baracchini et al. and Fritz et al.).

Further, regarding a compound 8 to 50 nucleobases in length targeted to a coding region of a nucleic acid molecule encoding human acyl CoA cholesterol acyltransferase-2 (SEQ ID NO: 3), as now recited in claim 1 and Applicant's arguments that Cases et al. and Sturley do not recite antisense compounds targeted to specific regions of acyl CoA cholesterol acyltransferase-2 and Baracchini et al and Fritz et al. do not teach the use of antisense compounds targeted to specific regions of acyl CoA cholesterol acyltransferase-2 (SEQ ID NO:3), Baracchini et al. teach antisense oligonucleotides that can specifically hybridize with a 5'-untranslated region, a stop codon region, a coding region, or a 3'-untranslated sequence of a target gene (see column 9, lines 6-67 and column 10, lines 1-25 and Table 1). Therefore, one of ordinary skill in the art would have been motivated and expected success to make an antisense compound targeting a specific region, such as the coding region, of a nucleic acid molecule encoding acyl CoA cholesterol acyltransferase-2 (SEQ ID NO:3) because it is well known in the art to target different sites

Art Unit: 1635

within a gene for the oligonucleotide interaction to occur such that a desired effect (e.g., detection or modulation of expression of the protein) will result. It is noted that there is no evidence of record to show any such differences between the acyl CoA cholesterol acyltransferase-2 sequence of Cases et al. (see Cases et al. SEQ ID NO: 4) and SEQ ID NO:3 of the instant invention that would have resulted in an artisan not being able to successfully design and use antisense oligonucleotides targeted to different sites/regions of acyl CoA cholesterol acyltransferase-2 (SEQ ID NO:3) of the instant invention.

Conclusion

Claims 1, 2, and 4-14 remain rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

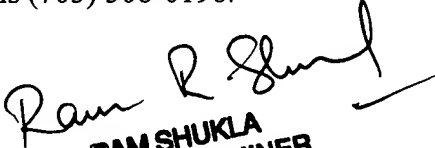
Art Unit: 1635

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-8693 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

tcg
April 9, 2003


RAM SHUKLA
PRIMARY EXAMINER